

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number  
**WO 2004/042365 A3**

- (51) International Patent Classification<sup>7</sup>: C12Q 1/68, C07H 21/04
- (21) International Application Number: PCT/US2003/036247
- (22) International Filing Date: 3 November 2003 (03.11.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/423,113 1 November 2002 (01.11.2002) US
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
- with international search report
  - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 24 February 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DEVELOPMENT OF THERAPEUTICS FOR THE TREATMENT OF ENDOTOXIN-MEDIATED DISEASES

(57) Abstract: The subject invention comprises a method for identifying an evolutionarily meaningful nucleotide change in a primate's *TLR4* polynucleotide. It further comprises methods for identifying agents that interact with the corresponding evolutionarily meaningful amino acid change so as to modulate the function of the *TLR4* polypeptide, thereby attenuating activation of the NF- $\kappa$ B pathway. Such agents are useful in mitigating the LPS mediated response and in the treatment of sepsis, severe sepsis and septic shock.

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